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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,380	01/26/2004	Maurice M. Moloney	9369-292	4979

1059 7590 07/01/2008

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EXAMINER	
RAGHU, GANAPATHIRAM	
ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
07/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/763,380	MOLONEY ET AL.	
	Examiner	Art Unit	
	GANAPATHIRAMA RAGHU	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-69* is/are pending in the application.

4a) Of the above claim(s) *51-55,62,68 and 69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-50, 56-61 and 63-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Application Status

In response to the Office Action mailed on 10/16/2007, applicants' filed a response and a terminal disclaimer on 04/16/2008. Said response, amended claims 42, 53, 60 and 61. Claims 42-69 are pending in this application, claims 51-55, 62, 68 and 69 remain withdrawn as they are drawn to non-elected inventions. Claims 42-50, 56-61 and 63-67 are now under consideration.

The terminal disclaimer filed on 04/16/2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of the following patents; U.S. Patent No. 5,650,554, U.S. Patent No. 5,948,682, U.S. Patent No. 6,288,304 B1 and U.S. Patent No. 6,753,167 B2, has been reviewed and is accepted. The terminal disclaimer has been recorded.

Applicants in their response have traversed the withdrawal of claims 51-55 and 62 with the arguments "that election of species does not limit the scope of the claim but rather provides a starting point for the examiner search. Based on the examiner's objections discussed below, it appears that the examiner has examined the full scope of the claims and therefore applicant should not be requested to withdraw claims 51-55 and 62". Applicants' arguments have been considered and are found to be non-persuasive for reasons stated in FAOM of letter dated 10/16/2007. Group I invention comprises structurally varied and distinct molecules that have either different structures or encode genes with different structures and are patentably distinct, searching for all the species would impose a serious search burden and furthermore even the elected claims 42-50, 56-61 and 63-67 and the species carp-growth hormone are not in

condition for the allowance. Contrary to applicants' arguments, for the clearly cited reasons, searching of all species in Groups I is a serious search burden and pursuant to 35 U.S.C. 121, 37 CFR 1.143 and 37 CFR 1.499, examiner is required to examine the elected invention.

Objections and rejections not reiterated from previous action are hereby withdrawn.

Withdrawn-Double Patenting rejection

Previous rejections of the following claims:

1) Claims 42-50, 55, 58-60, 61 and 63-67 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 16, 29, 31 and 32 of prior U.S. Patent No. 5,650,554,

2) Claim 57 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 16, 29, 31 and 32 of prior U.S. Patent No. 5,650,554,

3) Claims 42-50, 55, 56, 58-60, 61 and 63-67 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 13-19 and 21-26 of prior U.S. Patent No. 6,753,167 B2,

4) Claim 57 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 13-19 and 21-26 of prior U.S. Patent No. 6,753,167 B2,

5) Claims 42-50, 55, 58-60, 61 and 63-67 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 12-15 and 17-19 of reference patent U.S. Patent No. 5,948,682,

6) Claim 57 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 12-15 and 17-19 of reference patent U.S. Patent No. 5,948,682,

7) Claims 42-46, 55, 56, 58, 59, 60, 61, 63 and 65-67 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 and 9-11 of reference patent U.S. Patent No. 6,288,304 B1,

8) Claims 47-50 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 and 9-11 of reference patent U.S. Patent No. 6,288,304 B1, and

9) Claim 57 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 and 9-11 of reference patent U.S. Patent No. 6,288,304 B1,

Is being withdrawn in view of the submission of terminal disclaimer filed by the applicants.

Maintained-Claim Rejections: 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 42 (claims 43-52 and 56-59 depending therefrom), claim 60 and claim 61 (claims 62-67 depending therefrom) are rejected under 35 U.S.C. 112, second

paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 42, 60 and 61 is rejected for the phrase "sufficient portion", as the metes and bounds encompassed by the claim are not clear. What are the structural and functional limitations encompassed and is considered to be "sufficient portion" of the elected oil body protein oleosin? Perusal of the specification did not yield a definition for "sufficient portion". Clarification and correction is required.

In support of their request that the prior rejection of Claim 42 (claims 43-52 and 56-59 depending therefrom), claim 60 and claim 61 (claims 62-67 depending therefrom) be withdrawn, applicants provide the following argument:

(A) Applicants refer to page 22, line 23 through to page 23, line 2. One in the skill of art would readily understand what is meant by the phrase, especially with reference to the application.

(B) Further, this phrase is used in 8 issued patents to the applicant and therefore it was not deemed indefinite by the Patent Office in those cases.

Applicant's arguments have been fully considered but they are not persuasive and are answered as follows:

Reply (A): Perusal of the said sections in the specification indicates the following:

"The amino acid sequence necessary to provide targeting to the oil body for *Arabidopsis thaliana* oleosins contain amino acids 46-117 shown in SEQ ID NO: 2. Similarly, the amino acid sequence necessary to provide targeting to the oil body for

Brassica napus oleosins contains amino acids 60-132 shown in SEQ ID NO: 5. In a preferred embodiment, the amino acid sequence necessary for targeting additionally contains the N-terminus of the oleosin which includes amino acids 1-45 (SEQ D NO: 2) and 1-60 (SEQ ID NO: 5) for *Arabidopsis* and *Brassica* respectively.

Claims are interpreted in the light of the specification and specification cannot be read into the claims. Furthermore, claims are given the broadest reasonable interpretation and this interpretation is supported by what is disclosed in the specification and thus it is very clear from the specification (i) that the minimal structure requirement for efficient targeting of an oil body protein varies from one oleosin to the other i.e., SEQ ID NO: 2 of *Arabidopsis* and SEQ ID NO: 5 of *Brassica* and the requirement; (ii) the cited sections in the specification do not explicitly state both amino terminal and hydrophobic core region are required for efficient targeting; (iii) in the light of the above information provided in the specification, it is interpreted as specific structural regions for efficient targeting of any given oleosin must be defined to enable one of skill in the art to practice the invention; and (iv) therefore in the absence of defined specific structural details of any given oleosin protein, claims are deemed to be indefinite as it is unclear which specific oleosin is being claimed and the minimal structural requirement of said oleosin for efficient targeting i.e., does it encompass hydrophobic core region alone or both amino terminal and hydrophobic core region.

In addition, applicants in support of the withdrawal of the 102 (b) and 103 (a) rejections in the parent application 08/366,783 that has matured into a patent US Patent No.: 5,650,5554 (date of patent 07/22/97), applicants' had argued specifically to

overcome the rejection based on the reference of Qu et al., (J. Biol. Chem., Vol. 265: 2238-2243) by the submission of a declaration by inventor Maurice Moloney that the prediction by Qu et al., is incorrect and in order to demonstrate that the central hydrophobic core alone (which Qu et al., define to be amino acids 49-126) is not sufficient to provide targeting. Maurice Moloney declaration demonstrates "that if amino acids 2-47 of the N-terminus are deleted, then there is substantial reduction in targeting to the oil bodies and drastic reduction in protein stability. These results disprove the predictions of Qu et al., and demonstrate the unexpectedness of the results of the present invention". The said declaration goes on to argue that central hydrophobic region alone is not sufficient to provide targeting to an oil body.

When seen in the light of applicants' arguments in the parent application 08/366,783 the information provided in page 22, line 23 through to page 23, line 2 of the instant application, it is unclear what is "sufficient portion", as it can be interpreted to comprise the hydrophobic core alone of SEQ ID NO: 2 and 5 or it could also in addition comprise the N-terminus of SEQ ID NO: 2 and 5 and as such the claims are indefinite.

Reply (B): Examiner is not in a position to comment on the validity of what has been granted in previous patents and the interpretation of the claims are determined on a case by case basis and when the instant claims are given the broadest reasonable interpretation in the light of the specification, examiner continues to hold the position that claim language as written, the metes and bounds are unclear.

Maintained-Claim Rejections: 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 42-50, 56-61 and 63-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for a chimeric nucleic acid sequence encoding a fusion polypeptide comprising the full length oil body protein oleosin (polynucleotide of SEQ ID NO: 1 encoding the polypeptide of SEQ ID NO: 2) comprising a cleavable linker and a heterologous polypeptide (as in claims 61 and 63-67) and to a method of producing said chimeric fusion polypeptide in a host cell (as in claims 42-50 and 56-60), does not reasonably provide enablement for any chimeric nucleic acid sequence encoding a fusion polypeptide comprising any nucleic acid sequence that encodes a "sufficient portion" of an oil body protein or any oleosin of undefined structure necessary for the functional activity of said oil body protein, said fusion protein further comprising a cleavable linker and a polynucleotide encoding heterologous polypeptide and to a method of producing said chimeric fusion polypeptide in a host cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with the claim.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 42-50, 56-61 and 63-67 are so broad as to encompass any chimeric nucleic acid sequence encoding a fusion polypeptide comprising any nucleic acid sequence that encodes a "sufficient portion" of an oil body protein or any oleosin of undefined structure necessary for the functional activity of said oil body protein, said fusion protein further comprising a cleavable linker and a polynucleotide encoding heterologous polypeptide and to a method of producing said chimeric fusion polypeptide in a host cell. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of fusion-polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein encoded by a polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires knowledge and guidance with regard to which amino acids in the protein's sequence and the respective codons in its polynucleotide, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function. However, in this case the disclosure is limited to the use of a chimeric nucleic acid sequence encoding a fusion polypeptide comprising the full length oil body protein oleosin (polynucleotide of SEQ ID NO: 1 encoding the polypeptide of SEQ ID NO: 2) comprising a cleavable linker and a heterologous polypeptide (as in claims 61 and 63-67) and to a method of producing said chimeric

fusion polypeptide in a plant host cell (as in claims 42-50 and 56-60), but provides no guidance with regard to the making of variants and mutants of any oil body protein or any oleosin linked via cleavable linker to a heterologous polypeptide and to a method of expression in any host cell or with regard to other uses. In view of the great breadth of the claims, amount of experimentation required to make the claimed polypeptides the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Whisstock et al., Q Rev Biophys. 2003 Aug; 36(3): 307-340), the claimed invention would require undue experimentation. Further, Li et al., (J. Biol. Chem., 2002, Vol. 277 (40): 37888-37895) teach: **i)** that there are more than 40 different oleosins, comprising a characteristic central hydrophobic domain of ~70-75 uninterrupted and uncharged residues that forms an hairpin loop around three conserved proline residues around which flanked by relatively polar C-terminal (~65 residues) and N-terminal domains (~50 residues) and these domains are diverse in amino acid structure (Column 2, second paragraph, page 37888 and Column 2, Discussion, page 37892); **ii)** difficulty in expressing the central domain (hydrophobic domain) in *E.coli*, yeast and cell-free translation system (in fact, even the applicants' in the instant application have admitted on record that that the activity observed for fusion product is less than the unfused product when expressed in *E.coli*, Example 17: pages 62-64 of specification); **iii)** results from said study indicated that the maximum stability of reconstituted oil body emulsion is only possible with the intact oleosin protein and surface oriented amphipathic N- and C-terminal domains may play an important role in emulsion formation (column 1, second paragraph, page 37894); and **iv)** identical oleosin

molecules can interact to form homo-oligomers, some of which remain associated even in the presence of strong denaturants, such as SDS. Therefore, the specification fails to teach one of ordinary skill how to make and use the full scope of the fusion polypeptides encompassed by the claims.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is not routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions or deletions.

The specification does not support the broad scope of the claims for any chimeric nucleic acid sequence encoding a fusion polypeptide comprising any nucleic acid sequence that encodes a "sufficient portion" of an oil body protein or any oleosin of undefined structure necessary for the functional activity of said oil body protein, said fusion protein further comprising a cleavable linker and a polynucleotide encoding heterologous polypeptide and to a method of producing said chimeric fusion polypeptide in a host cell as claimed in claims 42-50, 56-61 and 63-67, because the specification does not establish: (A) regions of the protein/polynucleotide structure which may be modified without affecting the activity of any oil body protein or any oleosin; (B) the general tolerance of the polypeptide and the polynucleotide encoding any oil body

protein or any oleosin to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue or the respective codon in the polynucleotide with an expectation of obtaining the desired biological function with regards to any oil body protein or any oleosin; (D) said variant fusion polypeptides adopting a molecular configuration (as amphipathic N- and C- terminal portion/domains and central hydrophobic domain are required for the stable configuration of the oil body protein, such that the cleavable site is accessible to by protease factor Xa; (E) said variant fusion polypeptides adopting a molecular configuration with desirable properties and expressed to desirable levels in a host cell and presence or absence of necessary molecular chaperones that are necessary to express and proper folding of the fusion polypeptides in a host cell and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claim broadly including methods of using polypeptides with an enormous number of modifications. The scope of the claim must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any chimeric nucleic acid sequence encoding a fusion polypeptide comprising any nucleic acid sequence that encodes a "sufficient portion" of an oil body protein or any oleosin of undefined structure necessary for the functional activity of said oil body protein, said fusion protein further comprising a cleavable linker and a polynucleotide encoding heterologous polypeptide and to a

method of producing said chimeric fusion polypeptide in a host cell is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In support of their request that the prior rejection of claims 42-50, 56-61 and 63-67, under 35 U.S.C. 112, first paragraph for enablement, applicants provide the following arguments.

(A) As mentioned above, the term "sufficient portion" when used in relation to an oil body protein being able to target to a lipid phase would be readily understood... this term has been allowed in at least 8 patents.

(B) One of skill in the art readily determine what portion or fragment of an oil body protein would be "sufficient"... if the oil body protein was obtained from a plant, one would know that the hydrophobic central domain of the oil body protein would be necessary to provide targeting to the oil body...the specification also teaches that the N-terminus of the plant oil body protein should be included.

(C) Li et al., states on page 37888, last 4 lines of second column, that "oleosins have recently been proposed as a carrier for expression of purification of recombinant pharmaceutical peptides and industrial enzymes... therefore, Li et al., confirms the function of oil body proteins in targeting recombinant polypeptides to a lipid body.

(D) The examiner is of the opinion that the application is only enabling for preparing a recombinant polypeptide in a plant host cell.

Reply (A) & (B): As argued by the examiner in maintaining the 112, second paragraph the information provided in page 22, line 23 through to page 23, line 2 of the instant application, it is unclear what is "sufficient portion", as it can be interpreted to comprise the hydrophobic core alone of SEQ ID NO: 2 and 5 or it could also in addition comprise the N-terminus of SEQ ID NO: 2 and 5 and as such the claims are indefinite. Thus it is unclear to one of skill in the art that what portion or fragment of an oil body protein would be "sufficient"... if the oil body protein was obtained from a plant, what portion of the oil body protein should a chimeric protein must comprise for efficient targeting. Furthermore, the broadest interpretation of claims encompasses a genus of "oil body" proteins including varaints and mutants with any structure and clearly constitutes undue experimentation as it would involve making and testing many parent sequences including the mutants, variants and recombinants of said parent sequences with regard to the "sufficient portion" of the oil body protein to be comprised in a chimeric fusion protein as the putative amino terminal and caboxy terminal regions show a great diversity among various oil body proteins (Li et al.,).

Reply (C): Examiner is not disputing the fact that the oil body proteins can be used in targeting recombinant polypeptides as stated by Li et al., and has demonstrated in the instant application. Examiner's arguments are directed towards the breadth and scope of the claims as written. In addition, applicants attention is directed to Li et al., wherein it is clearly stated on page 37894, column 2, last paragraph "Our results also indicated that maximum stability of reconstituted oil body emulsions was only attained by reconstitution of the intact oleosin with oil bodies. The 9-kDa central core domain was

relatively poor emulsifying and stabilizing agent. The surface-oriented N- and C-terminal domains play an important role in emulsion formation...". In the light of this teaching by Li et al., a skilled artisan requires the structure of a parent sequence, as any changes in the N- and C-terminal domain is shown to affect the stability of the oil body protein.

Reply (D): Applicants arguments are persuasive and hence examiner has amended the rejection accordingly.

Written Description

Claims 42-50, 56-61 and 63-67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 42-50, 56-60 and 63-67 are directed to any chimeric nucleic acid sequence encoding a fusion polypeptide comprising any nucleic acid sequence that encodes a "sufficient portion" of an oil body protein or any oleosin of undefined structure necessary for the functional activity of said oil body protein, said fusion protein further comprising a cleavable linker and a polynucleotide encoding heterologous polypeptide and to a method of producing said chimeric fusion polypeptide in any host cell.

Claims 42-50, 56-60 and 63-67, are rejected under this section 35 U.S.C. 112, because the claims as interpreted, are directed to a genus of polynucleotides and encoding fusion polypeptides and to a method of making said fusion polypeptide that involves a genus of polynucleotides and encoding polypeptides with no support in the specification for the structural details associated with the function i.e., any chimeric

nucleic acid sequence encoding a fusion polypeptide comprising any nucleic acid sequence that encodes a "sufficient portion" of an oil body protein or any oleosin of undefined structure necessary for the functional activity of said oil body protein, said fusion protein further comprising a cleavable linker and a polynucleotide encoding heterologous polypeptide and to a method of producing said chimeric fusion polypeptide. No description of identifying characteristics of all of the sequences of an isolated polynucleotide encoding a fusion polypeptide of any oil body protein or any oleosin including variants, mutants and recombinants, has been provided by the applicants in the specification. No information, beyond the characterization of an isolated chimeric nucleic acid sequence encoding a fusion polypeptide comprising the full length oil body protein oleosin (polynucleotide of SEQ ID NO: 1 encoding the polypeptide of SEQ ID NO: 2) comprising a cleavable linker and a heterologous polypeptide (as in claims 61 and 63-67) and to a method of producing said chimeric fusion polypeptide in host cell (as in claims 42-50 and 56-60) has been provided by the applicants in the specification. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed. This recitation fails to provide a sufficient description of the claimed genus of polypeptides as it merely describes the functional features of the genus without providing any definition of the structural features of the species within the genus.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject

matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In support of their request that the prior rejection of claims 42-50, 56-61 and 63-67, under 35 U.S.C. 112, first paragraph for written description be withdrawn, applicants' have essentially provided the following argument.

(A) Examiner is of the opinion that the application as filed does not provide an adequate written description of "sufficient portion" of an oil body protein or any oleosin of undefined structure necessary for the functional activity of said oil body protein. Applicant is not attempting to claim any portion of an oil body protein per se, but is rather claiming a method of preparing a heterologous polypeptides by using sufficient portion of the oil body protein.

(B) Applicant has demonstrated actual reduction to practice of the claimed method using three oil body proteins.

(C) The examiner is of the opinion that the application as filed does not have an adequate written description for any host cell.

Reply (A) & (B): The reply given by the examiner regarding the definition provide by the examiner for maintaining 112, second paragraph rejection and 112, first paragraph rejection for enablement fully applies to the written description rejection also, the broadest interpretation of claims encompasses a genus of "oil body" proteins including variants and mutants with any structure and clearly constitutes undue experimentation as it would involve making and testing many parent sequences including the mutants, variants and recombinants of said parent sequences with regard to the "sufficient portion" of the oil body protein to be comprised in a chimeric fusion protein as the putative amino terminal and caboxy terminal regions show a great diversity among various oil body proteins (Li et al.,). Li et al., also clearly state on page 37894, column 2, last paragraph "Our results also indicated that maximum stability of reconstituted oil body emulsions was only attained by reconstitution of the intact oleosin with oil bodies. The 9-kDa central core domain was relatively poor emulsifying and stabilizing agent. The surface-oriented N- and C-terminal domains play an important role in emulsion formation...". In the light of this teaching by Li et al., a skilled artisan requires the structure of a parent sequence, as any changes in the N- and C-terminal domain is shown to affect the stability of the oil body protein.

Reply (C): Applicants arguments are persuasive and hence examiner has amended the rejection accordingly.

Summary of Pending Issues

The following is a summary of issues pending in the instant application.

1) Claim 42 (claims 43-52 and 56-59 depending therefrom), claim 60 and claim 61 (claims 62-67 depending therefrom) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

2) Claims 42-50, 56-61 and 63-67 are rejected under 35 U.S.C. 112, first paragraph, for enablement and written description.

Conclusion

None of the claims are allowable. Claims 42-50, 56-61 and 63-67 are rejected for the reasons identified in the Rejections and Summary sections of this Office Action. Applicants must respond to the objections/rejections in each of the sections in this Office Action to be fully responsive for prosecution.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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